

MAMMALIAN TWO-HYBRID SYSTEM FOR SCREENING FOR MODULATORS OF THE ACCUMULATION OF METABOLIC PRODUCTS

ABSTRACT OF THE DISCLOSURE

This invention utilizes a two-hybrid system to screen for agents that modulate the ability of a cell to degrade or to accumulate a metabolic product or to selective kill a cell or to selectively express a gene or cDNA in a cell that has a defect in its ability to degrade or to accumulate a metabolic product. One embodiment provides a mammalian cell comprising a nucleic acid encoding a peptide binding domain and an effector gene; a first chimeric protein comprising a nucleic acid binding domain that binds the peptide binding domain attached to the metabolic product or to a ligand that binds to the metabolic product; and a second chimeric protein comprising an expression control protein attached to the metabolic product or to the ligand that binds to the metabolic product such that when the first chimeric protein comprises the metabolic product, the second chimeric protein comprises the ligand and when the first chimeric protein comprises the ligand, the second chimeric protein comprises the metabolic product. The cell is contacted with a test agent and an alteration of expression of the effector gene is detected (if present) where a change in expression of the effector gene in response to the test agent indicates that the test agent modulates the ability of the cell to accumulate or degrade the metabolic product.